WHAT IS CLAIMED IS:

1. A method of generating a humanized animal, comprising:

recombining a first DNA construct with a second DNA construct,

wherein the first DNA construct has a non-human animal DNA sequence contained therein, and wherein the second DNA construct has a human DNA sequence contained therein and the human DNA sequence is flanked by a first and a second non-human animal DNA sequence;

isolating a recombined third DNA construct having a human DNA sequence flanked by the first and second non-human animal DNA sequence; and

introducing the recombined third DNA construct into a non-human embryogenic stem cell.

2. The method of claim 1, further comprising introducing the embryogenic stem cells into a non-human blastocyst and introducing the chimeric blastocyst into a pseudopregnant non-human animal.

3. The method of claim 1, wherein the first DNA construct is a bacterial artificial chromosome.

4. The method of claim 1, wherein the second DNA construct is a bacterial artificial chromosome.

5. The method of claim 4, wherein the bacterial artificial chromosome is linearized.

6. The method of claim 1, wherein the recombining is carried out in a strain of *E. coli*.

7. The method of claim 1, wherein the *E. coli* is deficient for *sbcB*, *sbcC*, *recB*, *recC* or *recD* activity and has a temperature sensitive mutation in *recA*.

8. The method of claim 1, wherein the human gene sequence is selected from the group consisting of genes encoding G-protein coupled receptors, kinases, phosphatases, ion channels, nuclear receptors, oncogenes, cancer suppressor genes, viral receptors, bacterial receptors, P450 genes, insulin receptors immunoglobins metabolic pathway genes, transcription factors, hormone receptors, cytokines, cell signaling pathway genes and cell cycle genes.

9. The method of claim 1, wherein the third DNA construct is a bacterial artificial chromosome.

10. The method of claim 1, wherein the human DNA sequence is a human gene sequence having at least one intron contained therein.

11. The method of claim 1, wherein the third DNA construct has a selection marker contained within the intron.

12. The method of claim 11, wherein the selection marker is added following the recombining step.

13. The method of claim 11, wherein the selection marker is a positive selection marker.

14. The method of claim 11, wherein the third DNA construct has a second selection marker that flanks the non-human animal DNA sequence.

15. The method of claim 1, wherein the non-human animal is a mouse and the non-human embryonic stem cells are mouse embryonic stem cells.

16. The method of claim 1, wherein the human DNA sequence and the first non-human DNA sequence in the second construct are joined to the 5' of a start codon in a human gene coding sequence.

17. The method of claim 16, wherein the human DNA sequence and the second non-human DNA sequence in the second construct are joined to the 3' of a stop codon in the human gene coding sequence.

18. A DNA construct for performing homologous recombination within a cell, the construct comprising:

a human DNA coding sequence having at least one intron disposed therein;

a selection marker gene contained within said at least one intron;

a first and second non-human animal DNA sequences flanking the human DNA, wherein the non-human animal flanking sequences are homologous to sequences in the genome of the non-human animal that flank a gene orthologous to the human DNA coding sequence.

19. The DNA construct of claim 18, further comprising a second selection marker adjacent to one of the non-human DNA sequences.

20. The DNA construct of claim 18, wherein the construct is a linearized bacterial artificial chromosome.

21. The DNA construct of claim 18, wherein the first and second non-human DNA sequences are mouse genomic DNA sequences.

22. The DNA construct of claim 18, wherein the flanking sequences are from about 0.1 to 200 kb in length.

23. The DNA construct of claim 18, wherein human DNA coding sequences and the first non-human sequence are joined adjacent to the 5' end of the start codon of the human DNA coding sequence.

24. The DNA construct of claim 18, wherein human DNA coding sequences and the first non-human sequence are joined adjacent to the 3' end of the stop codon of the human DNA coding sequence.

25. A method for generating a DNA construct for performing homologous recombination within a cell by

recombining a first DNA construct with a second DNA construct,
wherein the first DNA construct has a non-human animal DNA sequence contained therein, wherein the second DNA construct has a human DNA sequence contained therein and the human DNA sequence is flanked by a first and a second non-human animal DNA sequence;

isolating a recombined third DNA construct having a human DNA sequence flanked by the first and second non-human animal DNA sequence; and

introducing the recombined third DNA construct into a non-human embryogenic stem cell.

26. The method of claim 25, further comprising introducing the embryogenic stem cells into a non-human blastocyst and introducing the chimeric blastocyst into a pseudopregnant non-human animal.

27. The method of claim 25, wherein the first DNA construct is a bacterial artificial chromosome.

28. The method of claim 25, wherein the second DNA construct is a bacterial artificial chromosome.

29. The method of claim 28, wherein the bacterial artificial chromosome is linearized.

30. The method of claim 25, wherein the recombining is carried out in a strain of *E. coli*.

31. The method of claim 25, wherein the *E. coli* is deficient for *sbcB*, *sbcC*, *recB*, *recC* or *recD* activity and has a temperature sensitive mutation in *recA*.

32. The method of claim 25, wherein the human gene sequence is selected from the group consisting of genes encoding G-protein coupled receptors, kinases, phosphatases, ion channels, nuclear receptors, oncogenes, cancer suppressor genes, viral receptors, bacterial receptors, P450 genes, insulin receptors immunoglobins metabolic pathway genes, transcription factors, hormone receptors, cytokines, cell signaling pathway genes and cell cycle genes.

33. The method of claim 25, wherein the third DNA construct is a bacterial artificial chromosome.

34. The method of claim 25, wherein the human DNA sequence is a human gene sequence having at least one intron contained therein.

35. The method of claim 25, wherein the third DNA construct has a selection marker contained within the intron.

36. The method of claim 35, wherein the selection marker is added following the recombining step.

37. The method of claim 35, wherein the selection marker is a positive selection marker.

38. The method of claim 35, wherein the third DNA construct has a second selection marker that flanks the non-human animal DNA sequence.

39. The method of claim 25, wherein the human DNA sequence and the first non-human DNA sequence in the second construct are joined to the 5' of a start codon in a human gene coding sequence.

40. The method of claim 39, wherein the human DNA sequence and the second non-human DNA sequence in the second construct are joined to the 3' of a stop codon in the human gene coding sequence.

41. A humanized animal produced by the method of claim 1.

42. The humanized animal of claim 41, wherein the animal is a mouse.